

RECENT ADVANCES IN THE DIAGNOSIS AND TREATMENT OF HAY FEVER AND ASTHMA *

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The investigations of the last ten years have cleared the haze away from the asthma and hay fever problems, so that definite relief is now in store for most sufferers with these diseases. No one now can doubt the fact that these conditions are usually manifestations of protein sensitization or bacterial infection, since recent work shows that both bronchial asthma and hay fever may be due to susceptibility to one or several of the proteins in foods, pollens, animal hairs, bacteria, and several other substances like orris root.

Protein sensitization, moreover, has been shown to cause many cases of eczema and urticaria. All such conditions should be investigated with skin tests especially for foods, and also, if indicated for animal hairs and pollens as shown recently in Walker's article entitled "Causation of Eczema, Urticaria and Angino-Neurotic Edema." A recent case of eczema emphasizes the truth of this statement. In this case our skin tests showed marked susceptibility to most vegetables as well as to wheat, and there had been a vegetable diet prescribed, which, of course, had exaggerated the eczema.

These diseases, then, are the marked examples of protein sensitization, and internists today are wondering about the effect on the body of the slight but constant sensitivity to foreign proteins. Many of the obscure diseases, as suggested recently by Cooke, such as migraine, arthritis, chronic dyspepsia, renal and hepatic diseases may be associated with a chronic anaphylactic state. Gay and Southard have described the marked fatty and waxy changes of muscle, the local necrosis of epithelium, and the fibrous thickening of the glomerular capsule which results from acute anaphylaxis. It is, therefore, very probable that continued minimal anaphylactic shocks can work permanent damage. Therefore, for this added reason, the study of our present knowledge of protein sensitization is most important.

GENERAL CONSIDERATIONS

In the study of hay fever and asthma patients, a thorough diagnostic examination is the first essential to correct and successful management. We must be sure that the asthma is not associated with some lung, heart, kidney or other organic disturbance. Focal infections, especially in the sinuses, teeth, tonsils and pelvis must be discovered and cleared up. These cases, moreover, should all be examined, with the greatest care, by a competent nasal specialist and the remotest possibility of sinus infection ruled out. We feel, however, that operative procedures on the nose should not be done with the idea of a cure of hay fever or asthma without a careful diagnostic study by an internist, who can not only rule out the presence of organic disease, but also discover the presence or absence of protein sensitivity. Otherwise much unnecessary and sometimes dangerous nasal sur-

gery will be done as, for instance, in the case of a recent patient, who gave a most marked reaction to orris root, which is found in nearly all face powders, and where the nose had been thoroughly operated on from all angles, without the slightest relief.

To determine the fundamental cause of hay fever or asthma, skin tests with the various proteins of pollens, animal hairs, foods, bacteria, orris root and certain other substances in selected cases such as boxwood dust are absolutely necessary. These tests have been shown to be specific, and the whole procedure in the large part is out of the experimental stage, ready for the physician who wishes to give his asthmatic or hay fever patient as good and scientific treatment as is possible. In our work over 2,400 separate tests have been made on over ninety different patients and reactions have been obtained to nearly all kinds of foods, including fruits and vegetables. The technique of Walker and his suggestions as to the interpretations of the scarification method of skin testing have been followed explicitly since the intradermal method has certain disadvantages such as the danger of anaphylactic shock, the inability to do any large number of tests at any one sitting, and the inconstancy of some of the reactions. The so-called delayed reaction, which shows up twenty-four hours after the test with a tender, reddened area often slightly purulent, has been watched for in all cases. The very positive reactions present a most definite urticarial wheal with amœba like pseudo-podea and a red areola around about. We have obtained the most marked reactions with the pollen, animal hair, shell fish, wheat, and orris root proteins, though occasionally other proteins such as those of carrot and onion give striking results.

The manner in which these proteins produce their symptoms is a matter of the greatest conjecture. Why one person will have hay fever and another will have asthma from pollens, is surely a problem. Undoubtedly the cells of the entire epidermal covering of the body are sensitized to the proteins. Whether the asthma is due to a vagotonia or whether the mucous membrane of the bronchi becomes swollen and congested in the same way that the nasal mucosa does in hay fever is not settled.

Koessler feels that these conditions may be manifestations of a poisoning due to toxic amino acids which the body cells have split off from the proteins of pollens, food, bacteria, or animal hair. Thus, the unknown is ever stretching ahead of us in our medical studies.

HAY FEVER

That certain types of hay fever are caused by pollens was first suggested by Blackley in 1873 in "Experimental Researches on Hay Fever." He was able, to his own satisfaction, to explain the production of such symptoms by animal hair by the probable carrying of grass pollens in the fur of the animals, but his theory broke down when he attempted to explain the action of food in the production of this condition. In 1905, Dunbar proved that hay fever could be produced by the

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inhalation of pollen, and tried to treat patients with pollen injections. Since then, through the work of Noon and Freeman, Clowes, Goodale, Cooke, Koessler, Scheppegegrell, Walker, and Selfridge here in California, the present knowledge of the cause and treatment has evolved.

It is now certain that hay fever symptoms are due to susceptibility to proteins not only of pollens but of animal hairs, foods, bacteria, orris root and certain other substances. The patient's history will usually suggest which proteins are the most likely cause. However, though pollens cause most seasonal hay fever, certain of the summer coryzas, we have found are due to animal hairs and especially to bacteria. Again, bacteria or foods cause most of the all-year hay fevers, though it is well known that pollens may be at the basis of certain of these disturbances. Hence, no set rule can be laid down in regard to the character of the proteins which are to be used in testing any definite case. The physician doing this work must be prepared to test with all the proteins to which the patient is exposed.

For our work we have available the proteins of 86 foods, 8 animal hairs, 15 bacteria, 74 pollens, and that of several sachets, perfumes and orris root. The proteins of food, animal hair and bacteria have been purchased through commercial houses and they seem to be very satisfactory. As Selfridge³ has shown, however, the commercial pollens are useless for our work here in California, since this flora differs absolutely from that of the East, as shown by Professor Hall, and there are apparently many more hay fever-producing grasses and shrubs here than there. Hence, we have collected the pollens of the hay fever-producing grasses, shrubs, weeds and trees of this region of California ourselves, and have them available for diagnosis and treatment.

The recent articles of Walker have crystallized the thought on this subject, and we have conducted our work along lines suggested by him. He classifies the causes of hay fever and asthma in the following diagrammatic way:

Causes			
Sensitive		Non-Sensitive	
Seasonal	All year round	Seasonal	All year
Pollens	Hair	Bacteria	Bacteria
Foods	Food		
Bacteria	Bacteria		
Animal hair	Pollen		

Much difference of opinion exists at present, concerning the best method of diagnosis and treatment of hay fever due to pollens. Scheppegegrell thinks that one representative of each of his so-called biological groups of pollens is sufficient to use for diagnosis and immunizing purposes. Selfridge and probably Goodale, however, feel that there is a marked specificity for the individual pollens of the various species, and the former contends that immunization with each pollen to which the patient is susceptible is necessary for success. The hay fever pollens are probably much more profuse in California than in the East, and our own experience would indicate a marked specificity for each individual one.

For immunizing purposes, Walker and Goodale⁴

use strong dilutions finally in getting their good results, while Scheppegegrell⁵ and certain others recommend small doses. Our work confirms Walker's experience, and doses of strong dilutions are gradually administered, the dosage being controlled by skin tests. It is most gratifying to see the positive skin test to pollen protein gradually disappear with careful treatment. However, such immunity, it should be remembered, must be re-established each year, though it is hoped it may become permanent with successive immunizations. When the patient is sensitive to foods, removal of the food is usually effective. We have not attempted to immunize patients with hypodermic injections of wheat, but have recommended in several instances the gradual feeding of the offending food proteins, beginning with one-half milligram and working the dose gradually up to several grams. In regard to this food idiosyncrasy, we must remember, as Talbot has pointed out, that it often gives way to pollen or animal hair sensitiveness later in life. Horse dander susceptibility has been treated with gradually increasing doses of horse dander protein subcutaneously. Feather protein sensitivity has been taken care of by substituting floss pillows and mattresses for feather ones. Orris root symptoms require the use of rice powder if the patient is not sensitive to it, since nearly all commercial face powders contain orris root. Bacterial types of hay fever require the isolation from the sputum or nasal secretion of the offending organism and the preparation of an autogenous vaccine from it, especially if it is a streptococcus or any other organism than a staphylococcus or diphtheroid, in which latter cases Walker feels autogenous vaccines are not necessary.

To appreciate the results which can be obtained from such therapy, one must consult the most excellent articles of Walker entitled, "Frequent Causes and Treatment of Perennial Hay Fever" and "Sensitization and Treatment of Bronchial Asthmatics with Pollens."

We have made a study of twenty-six cases of hay fever seen in my private work, and in these cases there have been:

- 13 instances of seasonal pollen sensitiveness;
- 10 instances of bacterial sensitive and non-sensitive types;
- 6 instances of susceptibility to pollens, foods, and bacteria;
- 3 instances of sensitiveness to animal hairs as well as to pollens or bacteria;
- 9 instances of susceptibility to orris root;
- 1 instance of sensitiveness to beef protein;
- 2 instances of sensitiveness to chicken feathers alone.

To illustrate the diagnosis and treatment of seasonal hay fever due to pollens alone, the following case will be summarized:

E. M., a woman, age 30, has had hay fever of the most severe type for eighteen years, always from February to September. Constant running of eyes and nose, sneezing on arising in the morning, and for one-half to one-hour periods during

the day occur. Suffers with terrible dryness of the throat and itching of the nose and eyes. Cannot go out into the country or fields or even into the night air. Feels bloated and swollen at times as well as feverish, and often large wheals come out over body. All symptoms disappear on going to San Francisco or into the high Sierras. The father has had hay fever for forty years and many of his people have catarrh.

Cutaneous tests showed marked reactions to one to five hundred dilutions of the pollens of *Poa annua*, oats, canary grass, wheat, fescue, Kentucky blue grass, barley, rye, brome, velvet, beard grass, timothy, mugwort, oryzopsis, and moderate reactions to white top, sage brush, dock, rag weed and poverty weed.

Immunization given for two months last year, with gradually increasing doses of the dilutions of these pollen proteins, relieved her of her hay fever for the first time during July and August for years. She has gained thirty pounds and feels better than she has for years. She is now able to ride and walk in the country, and can go out at night.

Other cases of this type could be cited. Our experience, in brief, indicates that pollen hay fever can be relieved by correct immunization with pollen dilutions to which the patient is susceptible. It is possible, in our minds, that the pollens of certain flowers such as the daisy, aster and cineraria can cause hay fever, providing enough of the flowers are grown in a given locality. A patient's house was recently found to be surrounded by Shasta daisies to which pollen she gave a tremendous reaction, and even though other grasses were found to be positive, immunization to Shasta daisy as well as the grasses was carried out.

The non-sensitive seasonal bacterial type is illustrated by the following case:

R. B., a man, age 31, has had attacks of running of the nose, itching and congestion in nose, and sneezing lasting about one day. Attacks occur usually in the summer. Sweeping always brings on attacks, and they come with nearly every cold. Asthma may come with a cold for about two days.

Shell fish has always poisoned him. Lips, tongue and throat swell, stomach becomes unsettled, and he vomits and feels very ill after eating even a small amount.

Cutaneous tests with all the foods he eats except for shell fish as well as animal hairs, orris root, and pollens were entirely negative.

He, therefore, is an example of the seasonal non-sensitive bacterial type of hay fever, and will probably respond to the autogenous diphtheroid vaccine which we have prepared for his treatment.

A most interesting example of the sensitive bacterial all-year-round type of hay fever as well as of the marked horse dander hay fever is as follows:

G. G., a woman, age 21, has had sneezing every morning until noon for the last eight years, following a severe attack of bronchitis. Sneezing often is steady and lasts into the afternoon, and may awaken her at night for one-half to one hour. Nose runs terrifically, and nose and roof of mouth itch. Has tightness in her chest, and breathing is never easy. Feels tired and drowsy all the time. She also has had a typical hay fever and wheezing when she has been around horses, for the last three years. She becomes so ill and tired, and eyes and nose itch and run so much that she must go to bed after being around them.

Cutaneous tests were positive to staphylococcus albus and strongly positive to horse dander and horse-hair protein. To all other proteins her tests were negative. Cultures of her abundant nasal secretion showed a pure culture of staphylococcus albus, and three injections of the autogenous vaccine, prepared by my bacteriologist, Miss Margaret Eakin, relieved her completely. For three months she has been free from all symptoms. We are also immunizing her carefully to horse dander proteins, and feel confident that she will be able to be around horses again without trouble.

An example of food sensitiveness accompanying pollen susceptibility, follows:

A woman, age 30, has typical hay fever beginning in April and lasting through July. She is susceptible to several of the spring pollens, and also to many of the green vegetables. We feel that the limitation of these vegetables in her diet is most important. She is being immunized to the pollens to which she reacted.

A most striking example of orris root and non-sensitive bacterial hay fever, follows:

F. S., a woman, age 24, has had attacks of swelling of the nasal mucosa, marked coryza and watering of the eyes, marked swelling across the bridge of the nose and swelling of the eyes, for the last three years, coming every few days. She has been unable to use orris root as a shampoo, and is unable to ride on a street-car or go into a room with women who have used face powder. With severe attacks she gets marked throbbing in nose and over her eyes, and is so miserable that she has to go to bed. Her nose has been operated on several times, with no relief. During the last year her hay fever symptoms have persisted, and during the last few months she has been having asthma.

Cutaneous tests were negative to all proteins except orris root, to which she gave a tremendous reaction.

When she does not come in contact with face powder she is fairly comfortable, though her symptoms have persisted, probably due to a secondary nasal infection. We feel that when she is immunized to the staphylococcus aureus, which Miss Eakin has found in her sputum, she will get complete relief.

These examples of the various proteins which can cause hay fever, show the propriety of the suggestions of Cooke to call this disease "protein rhinitis." Our work confirms the idea of multiple sensitization and specificity of proteins in hay fever, and shows the futility of doing hay fever testing here, with anything except a full supply of California pollens, foods, hairs and bacteria. We feel that this work moreover, can best be carried out by a trained bacteriologist, who can make free and frequent use of bacteriology with the minimal expense to the patient.

ASTHMA

Meltzer probably first suggested, in 1910, that bronchial asthma is due to an anaphylactic state. In 1912, Schloss⁶ first demonstrated that specific sensitization to foods existed in man, and that the skin test could be used to determine this susceptibility. His work was extended by other investigators to urticaria and eczema and laid the foundation for the memorial series of studies, which Walker has published during the last four years.

In these twenty-seven or more articles, Walker reports his scientific investigations on his large

series of asthmatics and shows in careful detail the manner of treating nearly every type of case. No one interested in this subject should miss a careful study of all these articles.

His articles in the "Oxford Medicine" summarizes many points which are important to mention here.

Walker states that true bronchial asthma is an anaphylactic phenomenon, resulting from some foreign protein. Asthmatic bronchitis, however, is the result of prolonged respiratory infection and produces dyspnoea, bronchitis, and coughing at night due to the accumulation of a sticky sputum. Often asthmatic bronchitis is superimposed on true bronchial asthma, this occurring early in cases in children due to the susceptibility of their mucous membranes to infection.

Walker, as previously stated, uses the cutaneous skin tests rather than the intradermal one. A positive test for a protein may not mean that that protein is causing the asthma, but it does point out a danger which should be kept in mind. Omission of a food from the diet may desensitize a patient and change a positive test to a negative one. Hence, it is important to be eating the foods for which tests are done and to repeat slightly positive reactions. Bacteria may give a negative test for protein sensitiveness, but may still cause asthma due to their infectious nature alone.

Of six hundred asthmatics, Walker found 48 per cent sensitive to some protein, and 52 per cent non-sensitive. Sixteen per cent of the 600 were sensitive to animal emanations, mostly to horse protein. Twelve per cent were positive to foods, wheat, egg, potato and fish being the most frequent in succession. Ten per cent were positive to bacterial proteins, the staphylococcus aureus, streptococcus hemolyticus and hemolyticus, staphylococcus albus, and streptococcus viridans being the order of frequency. Micrococcus tetragenous, diphtheroid, and other bacteria also give positive reactions. Eleven per cent gave positive tests to pollens. Pollen asthmatics often have a secondary bacterial bronchitis.

Walker shows that as the age of onset of asthma increases, the frequency of sensitization decreases and the frequency of non-sensitiveness increases, the latter being universal after the age of fifty. After forty, occupations such as baking, tending horses, or sifting coffee beans are apt to bring on asthma due to the exposure to the specific proteins. Each sex, all ages, and all races are equally susceptible to asthma. The longer the duration of asthma, the more pronounced is the resultant bronchitis and emphysema and the more difficult the relief. Multiple sensitization occurs most frequently in youth and sensitization to one protein is apt to be followed by another later on. Eczema is usual in youth where a food susceptibility is present. Heredity was positive in about 48 per cent of all asthmatics.

In regard to treatment, Walker states that high temperature destroys anaphylactic properties of food so that toasted bread, baked potato or boiled

milk may be given to people susceptible to the proteins of these foods. Patients, moreover, may be able to eat small amounts, but not large amounts of certain foods. Eighty per cent of the sensitive cases are relieved by protein therapy, and another 10 per cent are relieved by vaccines. At least two-thirds of the non-sensitive asthmatics are relieved by vaccine therapy, or we must try another organism if the vaccine fails. Operations will not relieve the sensitive types, and surgery should only be done in the non-sensitive types to remove the foci of infection or promote drainage. Change of climate will help the non-sensitive patients, but not the sensitive ones, unless they are susceptible to pollens.

We will conclude our article with the analysis of thirty-eight cases of asthma, which have been referred to me in my private practice. Of these cases there have been:

- 23 cases of the sensitive and non-sensitive bacterial type.
- 6 cases of the bacterial and food sensitive type.
- 2 cases of the bacterial, food and animal hair type.
- 2 cases of animal hair type alone.
- 2 cases of the food type alone.
- 2 cases of the pollen and bacterial type.
- 2 cases of the pollen type alone.
- 1 case of the bacterial, food and pollen type.

A brief summary of some of the histories and methods of therapy will be given.

Three cases illustrative of the bacterial type of asthma will be summarized:

M. M., a woman, age 25, has had asthmatic wheezing continually since she was eight years old. Since the age of sixteen, it had been so distressing in the winter that she had to come from her home in Seattle to California. She has never raised any sputum. Severe attacks are frequent. She has been unable to ride horses for some years on account of the exaggeration of her asthma.

Cutaneous tests were negative with the exception of a moderately positive reaction to horse dander. X-rays of sinuses showed a right maxillary sinusitis and an abscess at the root of the first upper right bicuspid. The extraction of this tooth and drainage of the antrum together with several injections of pituitary and adrenalin extracts at the time eradicated the asthma, and she has been free for two years. Her susceptibility to horse dander proteins was not sufficient to give any symptoms unless in close contact with horses.

F. W., a woman, age 35, has had a dry hacking cough associated with a wheezing bronchitis with exaggerated spells of bronchial asthma with acute colds, continually for twenty years.

Cutaneous tests gave a marked reaction to streptococcus hemolyticus and were negative to all other proteins.

X-rays of teeth showed a definite apical infection of four teeth. These were extracted and her infected tonsils were removed also.

Cultures of the tonsils gave a pure culture of streptococcus hemolyticus and the asthma which persisted for two months after the teeth and tonsils were removed, cleared up when careful immunization with the vaccine was carried out. She has remained entirely free from her asthma for over one year.

This case shows the necessity of desensitizing the patient to the bacteria which is producing the trouble, especially when a specific skin test is

present, even after the harborers of the bacteria have been removed.

E. B., a woman, age 52, has had asthma following pneumonia nearly continuously for twenty-four years with exaggerated attacks with colds. Raises much sputum. Occasionally sneezing and running of the eyes and nose occurs.

Cutaneous tests were negative except to staphylococcus aureus and orris root. Cultures of the sputum yielded a pure diphtheroid and immunization has given her marked relief for the last eight months.

Two cases of combined food and bacterial sensitiveness will be mentioned:

M. W., a woman, age 40, has had bronchial asthma continuously since childhood. As a child had hives.

Cutaneous tests were positive to wheat proteins and to orris root. Cultures of sputum showed a streptococcus and diphtheroid. Cutting the wheat from her diet and immunizing her with the vaccine is giving her relief.

G. H., a boy, age 6, has had very severe attacks of bronchial asthma since the age of six months, when vegetables were first added to his diet. He has always been wheezy and unable to play or run.

Cutaneous tests were markedly positive to carrot, corn and onion proteins and to staphylococcus aureus. His sputum yielded a pure culture of staphylococcus aureus.

Elimination of carrots, corn and onions from the diet did not relieve his wheezing until immunization to an autogenous staphylococcus vaccine was carried out and since then he has had relief. For the first time in his life he is able to play and run like other boys.

These last two cases illustrate the type which is originally sensitized to food proteins and where asthma becomes chronic because of an added bacterial infection.

One example of asthma due to foods alone is given:

B. W., a boy, age 8, has had many frequent attacks of bronchial asthma for several years.

Cutaneous tests showed marked reactions to carrots, rice and peanuts. Dr. Clifford Sweet reports complete relief since these foods were eliminated, with the exception of a slight attack when he broke over his diet.

An interesting example of susceptibility to foods, pollen and bacteria is cited.

P. T., a boy, age 10, has had severe attacks of asthma every ten or twelve days for the last three years and has never been absolutely free from difficult breathing. He has very little sputum.

Cutaneous tests gave positive results with the pollens of Kentucky blue, poa annua, barley, wheat, agrostis, and timothy grasses. Tests for wheat proteins, as well as wheat glutenin, leucosin, and globulin, corn, barley and beef proteins showed marked so-called delayed reactions. All other reactions were negative.

Immunization to the pollens, together with the elimination of the foods to which he was sensitive, and immunization to an autogenous vaccine, consisting of a streptococcus, gram negative diplococcus and staphylococcus aureus has given definite and gratifying relief. He can now play ball for the first time since asthma began.

In conclusion, certain points should be emphasized to assure correct diagnosis and success in the treatment of cases of hay fever and asthma.

1. A complete stock of proteins of foods, animal hairs, orris root, bacteria, as well as a

large number of our California pollens is the first essential for correct diagnosis and treatment.

2. Ready access to a competent bacteriologist who can carefully prepare vaccines as needed for the treatment of these cases, is important.

3. The pollen type of hay fever receives marked relief by proper pollen therapy and this should be given with the local pollens only.

4. The bacterial types of asthma and hay fever receive striking and often rapid relief with autogenous vaccines.

5. Food types of these illnesses must be treated with absolute removal of the foods to which sensitivity exists to get results. Desensitization may then be tried.

6. Surgery is important if foci of infection are present or drainage is imperfect.

7. The writer feels that if care is taken and the patients co-operate, most of these sufferers can receive either partial or complete relief from hay fever and asthma.

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Prescribing Intoxicating Liquors—"The writing of prescriptions for intoxicating liquors for the fee or because the person is a good friend is not only illegal but dishonest, forfeits respect even from the recipient, and each time leaves the doctor one notch lower in self-respect."—(A. W. Abbott, Journal-Lancet, January, 1922.)

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